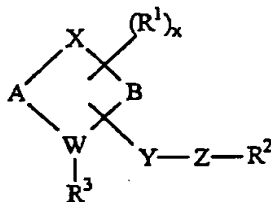


93

CLAIMS

1. A compound of the formula



wherein

5 A is $(\text{CH}_2)_m$, m being from 1 to 3;

B is $(\text{CH}_2)_n$, n being from 1 to 3;

x is from 0 to 2;

R¹ is C₁ to C₁₀ hydrocarbyl, in which up to 2 carbon atoms may be replaced by O, S or N, and up to 2 hydrogen atoms may be replaced by halogen;

10 R² is H or C₁ to C₁₅ hydrocarbyl, in which up to 3 carbon atoms may be replaced by O, S or N, and up to 3 hydrogen atoms may be replaced by halogen;

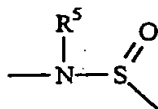
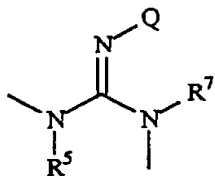
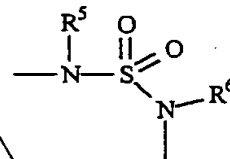
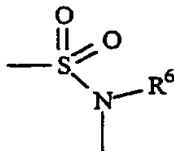
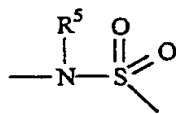
R³ is absent when -Y-Z-R² is attached to W, or is H or C₁ to C₇ hydrocarbyl when -Y-Z-R² is not attached to W;

15 W is nitrogen;

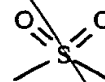
X is -CH₂-, -O- or -NR⁴-, R⁴ being H or C₁ to C₃ alkyl;

Y replaces a hydrogen atom on any of A, B, W and X, and is C₂ to C₁₀ alkylene, in which one non-terminal carbon atom may be replaced by O; and

20 Z is



or



wherein R⁵, R⁶ and R⁷ are independently H or C₁ to C₁₅ hydrocarbyl, in which up to 3 carbon atoms may be replaced by O or N, and up to 3 hydrogen

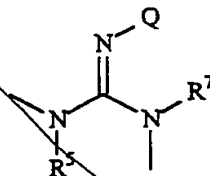
AMENDED SHEET

Sub
B1

0962544-101300

94

atoms may be replaced by halogen, and Q is H or methyl, or Q is linked to R⁵ or R⁷ to form a five-membered ring or Q is linked to R² to form a six-membered ring, provided that when Z is



- 5 at least one of R⁵ and R⁷ is aryl(C₁ to C₃)alkyl or cycloalkyl(C₁ to C₃)alkyl, optionally substituted by halo;
or a pharmaceutically acceptable salt thereof.

- 10 2. A compound according to claim 1 wherein R² is selected from alkyl, aryl, arylalkyl, cycloalkyl and cycloalkylalkyl, wherein alkyl moieties are optionally substituted by halo, and aryl groups are optionally substituted by C₁ to C₄ alkyl, C₁ to C₄ alkoxy or halo.
- 15 3. A compound according to claim 1 wherein R² is selected from phenyl, halophenyl, benzyl, halobenzyl, phenylethyl, halophenylethyl, phenylpropyl, halophenylpropyl, phenylbutyl, halophenylbutyl, tolyl, methoxybenzyl, trifluoromethylbenzyl, halo-methoxybenzyl, phenylbenzyl, adamantanemethyl, adamantaneethyl, adamantanepropyl, cyclohexanemethyl, cyclohexaneethyl, and naphthyl.
- 20 4. A compound according to any of claims 1 to 3 wherein x is 0.
- 25 5. A compound according to any of claims 1 to 3 wherein x is 1 or 2, and R¹ is selected from hydroxy, C₁ to C₉ alkoxy (optionally substituted by halo), C₁ to C₉ cycloalkylalkoxy (wherein the cycloalkyl group is optionally substituted by C₁ to C₄ alkyl or halo, and the alkoxy group is optionally substituted by halo), arylalkoxy (wherein the aryl group is optionally substituted by C₁ to C₄ alkyl, C₁ to C₃ alkoxy or halo, and the alkoxy group is optionally substituted by halo) and C₁ to C₉ alkylamino wherein the alkyl group is optionally substituted by halo.

95

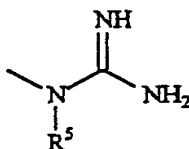
6. A compound according to any preceding claim wherein R^3 is H, C_1 to C_7 alkyl or benzyl

7. A compound according to any preceding claim wherein R^5 , R^6 and R^7 are independently selected from H, aryl(C_1 to C_3)alkyl and cycloalkyl(C_1 to C_3)alkyl, and are optionally substituted by halo.

8. A compound according to any preceding claim wherein Y is propylene, butylene, pentylene, hexylene, heptylene, octylene or nonylene.

9. A compound according to any preceding claim wherein $m+n \geq 3$.

10. A compound according to claim 8, wherein $m+n \geq 3$, $Z-R^2$ is



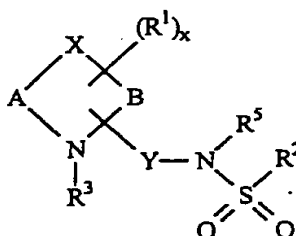
15 and R^5 is benzyl or halobenzyl.

11. ~~A compound according to any preceding claim, for use in therapy.~~

12. A compound which is degraded *in vivo* to yield a compound according to any of claims 1 to 10.

13. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any of claims 1 to 10, and a physiologically acceptable diluent or carrier.

14. A method of making a compound of the formula



AMENDED SHEET

Sub A1

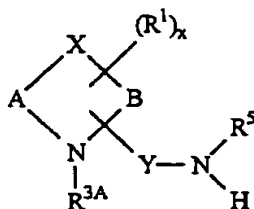
Sub A2

00622544-10300

29.02.00

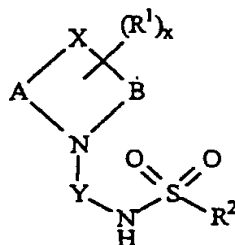
96

wherein A, B, x, R¹, R², R³, R⁵, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula R²SO₂Cl with a compound of the formula

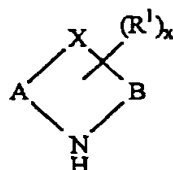


5 wherein R^{3A} is C₁ to C₇ hydrocarbyl or a protecting group.

15. A method of making a compound of the formula

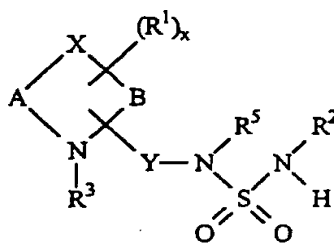


10 wherein A, B, x, R¹, R², X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula



with a compound of the formula Cl-Y-NH-SO₂-R².

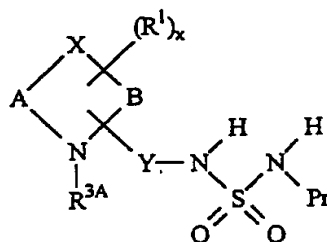
16. A method of making a compound of the formula



15

wherein A, B, x, R¹, R², R³, R⁵, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

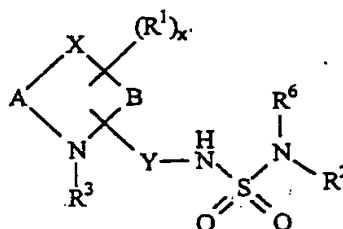
97



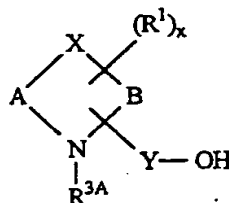
(wherein R^{3A} is C_1 to C_7 hydrocarbyl or a protecting group and Pr is a protecting group) with a compound of the formula R^2Br , and reacting the product with R^5Br when R^5 is not hydrogen.

5

17. A method of making a compound of the formula



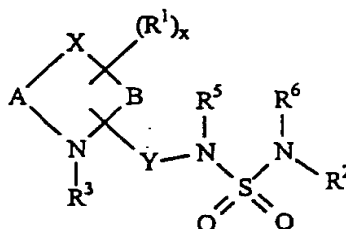
wherein A, B, x, R^1 , R^2 , R^3 , X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula



10

(wherein R^{3A} is C_1 to C_7 hydrocarbyl or a protecting group) with a compound of the formula $R^2-NH-SO_2-NH-Pr$, wherein Pr is a protecting group, and reacting the product with R^6Br when R^6 is not hydrogen.

15 18. A method of making a compound of the formula

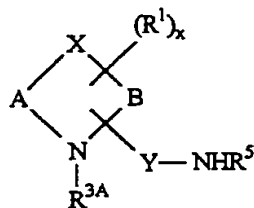


wherein A, B, x, R^1 , R^2 , R^3 , R^5 , R^6 , X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

AMENDED SHEET

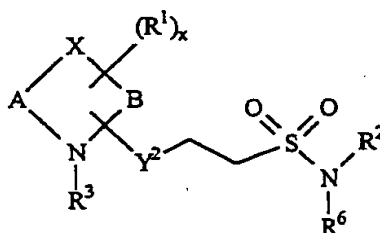
00522544-101300

98

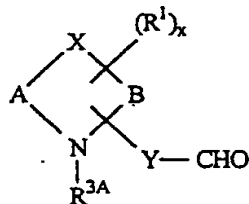


(wherein R^{3A} is C_1 to C_7 hydrocarbyl or a protecting group) with a compound of the formula R^2R^6NH and sulfamide.

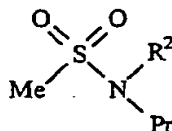
- 5 19. A method of making a compound of the formula



wherein A, B, x, R^1 , R^2 , R^3 , R^6 and X are as recited in claim 1 and Y^2 is a bond or C_1 to C_8 alkylene, said method comprising the step of reacting a compound of the formula



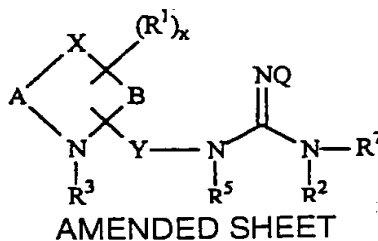
- 10 (wherein R^{3A} is C_1 to C_7 hydrocarbyl or a protecting group) with a compound of the formula



wherein Pr is a protecting group, reducing the reaction product, and (when R^6 is not hydrogen) reacting the reduced product with R^6Br .

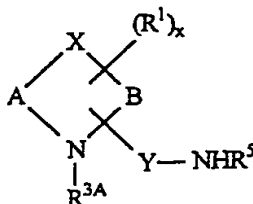
15

20. A method of making a compound of the formula

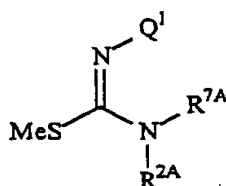


99

wherein A, B, x, R¹, R², R³, R⁵, R⁷, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula



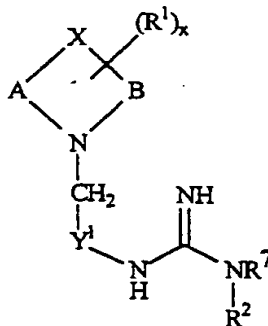
with a compound of the formula



5

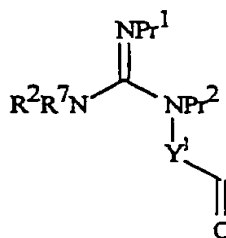
wherein Q¹, R^{2A}, R^{3A}, and R^{7A} are any of the groups defined for Q, R², R³, and R⁷, respectively, or protecting groups.

21. A method of making a compound of the formula



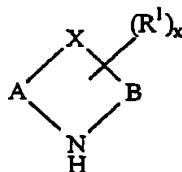
10

wherein A, B, x, R¹, R², and X are as recited in claim 1 and Y¹ is a C₁ to C₉ alkylene group, said method comprising the step of reacting a compound of the formula

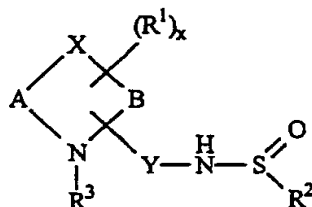


(wherein Pr¹ and Pr² are protecting groups) with a compound of the formula

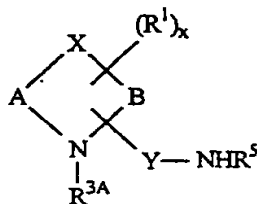
100 / 2502.00



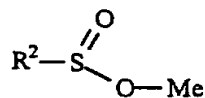
22. A method of making a compound of the formula



5 wherein A, B, x, R¹, R², R³, R⁵, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

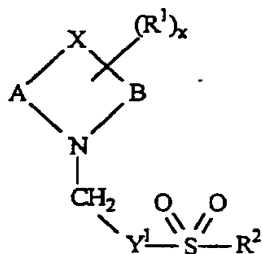


(wherein R³ᴬ is C₁ to C₇ hydrocarbonyl or a protecting group) with a compound of the formula



10

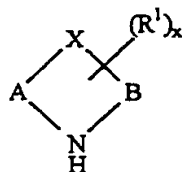
23. A method of making a compound of the formula



wherein A, B, x, R¹, R², and X are as recited in claim 1 and Y¹ is a C₁ to C₉ alkylene

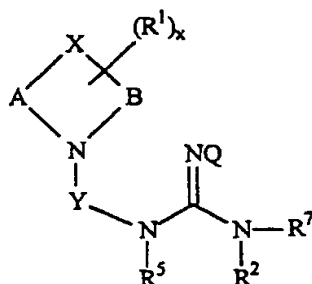
15 group, said method comprising the step of reacting a compound of the formula

101 29.02.00

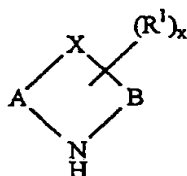


with a compound of the formula $R^2-SO_2-Y^1-CHO$.

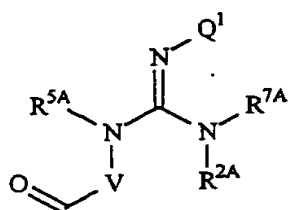
24. A method of making a compound of the formula



wherein A, B, x, R¹, R², R⁵, R⁷, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula



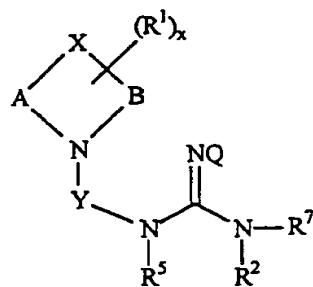
with a compound of the formula



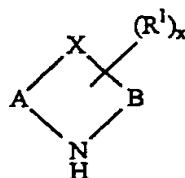
wherein V is C₁ to C₉ alkylene, and Q¹, R^{2A}, R^{5A} and R^{7A} are any of the groups defined for Q, R², R⁵ and R⁷, respectively, or a protecting group.

25. A method of making a compound of the formula

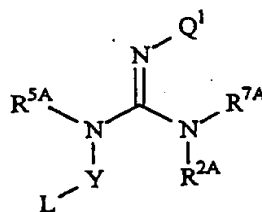
102



wherein A, B, x, R¹, R², R⁵, R⁷, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

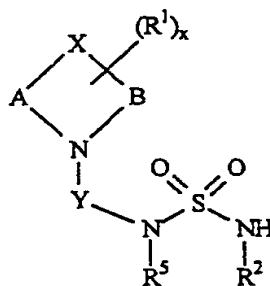


5 with a compound of the formula

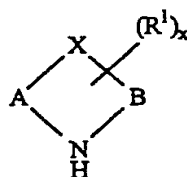


wherein L is a leaving group, and Q¹, R^{2A}, R^{5A} and R^{7A} are any of the groups defined for Q, R², R⁵ and R⁷, respectively, or a protecting group.

10 26. A method of making a compound of the formula



wherein A, B, x, R¹, R², R⁵, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

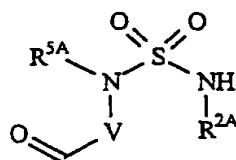


AMENDED SHEET

0962544-101300

103 29.02.00

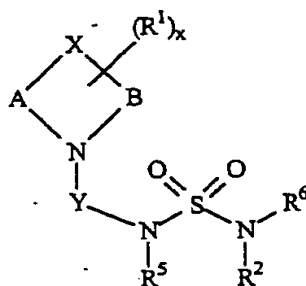
with a compound of the formula



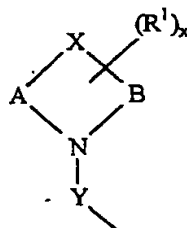
wherein V is C₁ to C₉ alkylene, and R^{2A} and R^{5A} are any of the groups recited for R² and R⁵, respectively, or a protecting group.

5

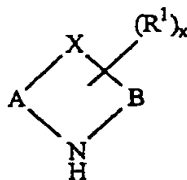
27. A method of making a compound of the formula



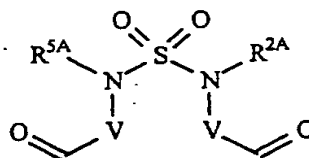
wherein A, B, x, R¹, R², R⁵, X and Y are as recited in claim 1 (provided that the moiety



10 constitutes a group falling within the definition of R⁶), said method comprising the step of reacting a compound of the formula



with a compound of the formula

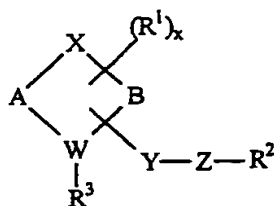


15 wherein V is C₁ to C₉ alkylene, and R^{2A} and R^{5A} are any of the groups recited for R² and R⁵, respectively, or a protecting group.

104

2902.00

28. The use of an H₃ receptor ligand in the manufacture of a medicament for modifying H₃ receptor activity in a patient, said H₃ receptor ligand being a compound of the formula



5 wherein

A is (CH₂)_m, m being from 1 to 3;

B is (CH₂)_n, n being from 1 to 3;

x is from 0 to 2;

10 R¹ is C₁ to C₁₀ hydrocarbyl, in which up to 2 carbon atoms may be replaced by O, S or N, and up to 2 hydrogen atoms may be replaced by halogen;

R² is H or C₁ to C₁₅ hydrocarbyl, in which up to 3 carbon atoms may be replaced by O, S or N, and up to 3 hydrogen atoms may be replaced by halogen;

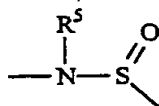
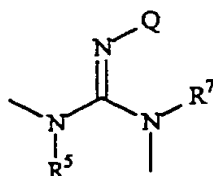
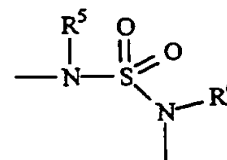
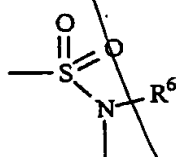
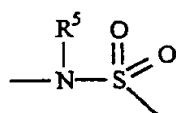
15 R³ is absent when -Y-Z-R² is attached to W, or is H or C₁ to C₇ hydrocarbyl when -Y-Z-R² is not attached to W;

W is nitrogen;

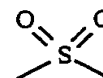
X is -CH₂-, -O- or -NR⁴-, R⁴ being H or C₁ to C₃ alkyl;

20 Y replaces a hydrogen atom on any of A, B, W and X, and is C₂ to C₁₀ alkylene, in which one non-terminal carbon atom may be replaced by O; and

Z is



or



105

2002.00

sub A3>

5

or a pharmaceutically acceptable salt thereof.

a dol
 β^2

add
c4

Table 1. Demographic characteristics of the study population	
Age (years)	65.2 ± 1.5
Gender (male/female)	102/108
Education (years)	12.5 ± 0.5
Marital status (married/divorced/widowed)	150/30/20
Occupation (retired/working)	150/30
Income (€ per month)	1,200 ± 100
Comorbidities (hypertension/diabetes/cholesterol)	120/40/60
Medication (antidepressants/antipsychotics)	80/20
Alcohol consumption (yes/no)	30/170
Smoking status (smoker/non-smoker)	40/160
Family history of mental illness (yes/no)	20/180
Duration of illness (years)	10.5 ± 2.0
Previous hospitalizations (yes/no)	50/150
Current symptoms (depression/anxiety)	100/100
Functional status (good/poor)	120/80
Quality of life (SF-36 score)	45.0 ± 5.0
Overall health status (good/poor)	100/100